

**JC13 Rec'd PCT/PTO 22 MAR 2002**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Matsumoto *et al.*

Art Unit:

Application No.

Filed: herewith

For: NOVEL GUANOSINE TRIPHOSPHATE-  
BINDING PROTEIN-COUPLED RECEPTORS  
AND GENES THEREOF, AND PRODUCTION  
AND USES THEREOF

Examiner:

Date: March 22, 2002

COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

**PRELIMINARY AMENDMENT**

Please enter this amendment before the fees are calculated.

**Please amend the specification as follows:**

On page 1, line 5 under the title, insert the following paragraph:

**--CROSS-REFERENCE TO RELATED APPLICATIONS**

This is the National Stage of International Application No. PCT/JP00/09408, filed December 28, 2000, which in turn claims the benefit of Japanese Application No. 11/375152 filed December 28, 1999 and Japanese Application No. 2000/101339, filed March 31, 2000.--

**Please amend the claims as follows.** Claims that have not been amended are denoted as reiterated for the examiner's convenience.

1. (Amended) An isolated DNA that encodes a guanosine triphosphate-binding protein-coupled receptor, wherein said DNA is selected from the group consisting of:

(a) an isolated DNA encoding a protein comprising an amino acid sequence of SEQ ID NOs: 1, 2, 3, 4, 17, 18, 19, 20, or 21;

(b) an isolated DNA comprising a coding region of a nucleotide sequence of any one of SEQ ID NOs: 5 to 8 and 22 to 26;

(c) an isolated DNA encoding a protein comprising the amino acid sequence of SEQ ID NOs: 1, 2, 3, 4, 17, 18, 19, 20, or 21 in which one or more amino acids are substituted, deleted, added, and/or inserted; and

(d) an isolated DNA hybridizing under stringent conditions to the DNA comprising the nucleotide sequence of SEQ ID NOs: 5, 6, 7, 8, 22, 23, 24, 25, or 26.

2. (Amended) An isolated DNA encoding a partial peptide of a protein comprising an amino acid sequence of SEQ ID NOs: 1, 2, 3, 4, 17, 18, 19, 20, or 21.

3. (Amended) A vector comprising the DNA of claim 1.

4. (Amended) A transformant comprising the DNA of claim 1.

5. (Amended) A protein or a peptide encoded by the DNA of claim 1.

6. (Amended) A method for producing a protein or a peptide encoded by the DNA of claim 1, comprising culturing a transformant comprising the DNA of claim 1, and recovering an expressed protein or peptide from the transformant or culture supernatant thereof.

7. (Amended) A method of screening for ligands that bind to the protein of claim 5, comprising:

(a) contacting a test sample including one or more compounds with the protein or the peptide of claim 5; and

(b) selecting the one or more compounds that bind to the protein or peptide, wherein the compounds are ligands of the protein of claim 5.

8. (Amended) A method of screening for compounds that have an activity of inhibiting binding between the protein of claim 5 and a ligand thereof, comprising:

(a) contacting the protein of claim 5 or a partial peptide thereof with the ligand in the presence of a test sample that includes one or more compounds and detecting a binding activity of the protein or partial peptide with the ligand; and

(b) selecting the one or more compounds that reduce the binding activity detected in step (a) as compared with a binding activity detected in the absence of the test sample.

9. (Amended) A method of screening for compounds that suppress or enhance the activity of the protein of claim 5 to transduce a signal into a cell *via* the activation of the G protein of claim 5, comprising:

(a) contacting a ligand of the protein of claim 5 with cells expressing the protein in the presence of a test sample including one or more compounds,

(b) detecting an alteration in the cells that results from binding of the ligand to the protein, and

(c) selecting the one or more compounds that suppress or enhance the alteration detected in step (b) as compared with an alteration detected in the cells in the absence of the test sample.

10. (Amended) The method of claim 9, wherein the alteration in the cells is a change in cAMP concentration or calcium concentration.

11. (Reiterated) An antibody binding to the protein of claim 5.

12. (Amended) A compound isolated by the method of claim 7.

13. (Reiterated) A pharmaceutical composition comprising the compound of claim 12 as an active ingredient.

14. (Reiterated) The pharmaceutical composition of claim 13, wherein said pharmaceutical composition is formulated for the treatment of a disease selected from the group consisting of cancer, cirrhosis, and Alzheimer's disease.

15. (Reiterated) A polynucleotide comprising at least 15 nucleotides, wherein said polynucleotide is complementary to the DNA comprising the nucleotide sequence of any one of SEQ ID NOs: 5 to 8 and 22 to 26 or a complementary strand thereof.

16. (Amended) A method for diagnosing a disease selected from the group consisting of cancer, cirrhosis, and Alzheimer's disease, comprising detecting expression of the DNA of claim 1 in tissues related to the disease derived from a subject, or mutation in the DNA of claim 1 in the subject.

17. (Amended) An agent for diagnosing cancer, cirrhosis, or Alzheimer's disease, wherein the agent comprises the antibody of claim 11.

**Please add the following new claims.**

18. (New) A vector comprising the DNA of claim 2.

19. (New) A transformant comprising the DNA of claim 2.

20. (New) A transformant comprising the vector of claim 4.

21. (New) A protein or a peptide encoded by the DNA of claim 2.

22. (New) A compound isolated by the method of claim 8.

23. (New) A compound isolated by the method of claim 9.

24. (New) A compound isolated by the method of claim 10.

25. (New) An agent for diagnosing a cancer, cirrhosis, or Alzheimer's disease, wherein the agent comprises the nucleotide of claim 15.

26. (New) The method of claim 7, wherein the method is a method of screening for ligands that suppress or enhance an ability of the peptide of claim 5 to transduce a signal into a cell via activation of the peptide of claim 5.

27. (New) The method of claim 8, wherein the method is a method of screening for ligands that suppress or enhance an ability of the peptide of claim 5 to transduce a signal into a cell via activation of the peptide of claim 5.

### REMARKS

By this amendment, claims 18-27 are added. Therefore, claims 1-27 are now pending. Claims 1-10, 12, and 16-17 were amended.

In addition, the cross-reference to related applications was added to the specification by this amendment.

Claims 1 and 2 were amended to comply with USPTO form, for example by inserting the term "isolated." Support for this amendment can be found on page 3, lines 14-19 and page 6, lines 8-14.

Claims 1, 6-9, 16 and 17 were amended to remove redundant claim language.

Claims 1, 2, 6-10 and 17 were amended to correct the antecedent basis.

Claims 3-6, 10, 12, and 17 were amended to remove the multiple dependency.

Claim 4 was amended to clarify the claim. Support for the amendment can be found on page 11, lines 19-30 of the specification.

Claims 7 and 8 were amended to clarify the claims. Support for the amendments can be found on page 14, lines 33-34 of the specification.

Claim 9 was amended to clarify the claim. Support for the amendment can be found on page 7, lines 1-5; page 16, lines 3-5; and page 18, line 28 – page 20, line 7 of the specification.

No claim was amended in view of any prior art. In addition, none of the amendments narrows the scope of any claim.

Claims 18-27 were added. Support for claim 18-25 can be found in the original multiple-dependent claim.

Claim 18: original claim 3;

Claims 19 and 20: original claim 4;

Claim 21: original claim 5;

Claim 22-24: original claim 12;

Claim 25: original claim 17; and

Claims 26 and 27: page 7, lines 1-5 and page 16, lines 3-5 of the specification.

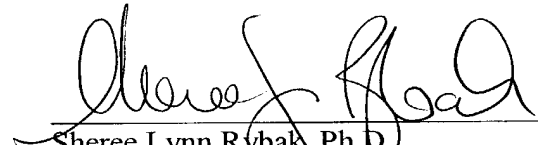
Therefore, no new matter is added by this amendment.

If there are any questions regarding this amendment, please telephone the undersigned at the telephone number below.

Respectfully submitted,

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**Marked-up Version of Amended Claims and Specification  
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)**

In the specification, page 1, line 5 under the title, insert the following paragraph:

**CROSS-REFERENCE TO RELATED APPLICATIONS**

This is the National Stage of International Application No. PCT/JP00/09408, filed December 28, 2000, which in turn claims the benefit of Japanese Application No. 11/375152 filed December 28, 1999 and Japanese Application No. 2000/101339, filed March 31, 2000.

In the claims:

1. (Amended) [A] An isolated DNA that encodes a guanosine triphosphate-binding protein-coupled receptor, wherein said DNA is selected from the group consisting of [the following (a) to (d)]:

(a) [a] an isolated DNA encoding a protein comprising [the] an amino acid sequence [of any one] of SEQ ID NOs: [1 to 4 and 17 to 21] 1, 2, 3, 4, 17, 18, 19, 20, or 21;

(b) [a] an isolated DNA comprising a coding region of [the] a nucleotide sequence of any one of SEQ ID NOs: 5 to 8 and 22 to 26;

(c) [a] an isolated DNA encoding a protein comprising the amino acid sequence of [any one of] SEQ ID NOs: [1 to 4 and 17 to 21] 1, 2, 3, 4, 17, 18, 19, 20, or 21 in which one or more amino acids are substituted, deleted, added, and/or inserted; and

(d) [a] an isolated DNA hybridizing under stringent conditions to the DNA comprising the nucleotide sequence of [any one of] SEQ ID NOs: [5 to 8 and 22 to 26] 5, 6, 7, 8, 22, 23, 24, 25, or 26.

2. (Amended) [A] An isolated DNA encoding a partial peptide of a protein comprising [the] an amino acid sequence of [any one of] SEQ ID NOs: [1 to 4 and 17 to 21] 1, 2, 3, 4, 17, 18, 19, 20, or 21.

3. (Amended) A vector comprising the DNA of [any one of] claim[s] 1 [and 2].

4. (Amended) A transformant [carrying] comprising the DNA of [any one of] claim[s] 1 [and 2 or the vector of claim 3].

5. (Amended) A protein or a peptide encoded by the DNA of [any one of] claim[s] 1 [and 2].

6. (Amended) A method for producing [the] a protein or [the] a peptide [of claim 5] encoded by the DNA of claim 1, [said method] comprising [the steps of] culturing [the] a transformant [of claim 4] comprising the DNA of claim 1, and recovering an expressed protein or peptide from the transformant or culture supernatant thereof.

7. (Amended) A method of screening for ligands that bind to the protein of claim 5, [said method] comprising [the steps of]:

(a) contacting a test sample[, ] including one or more compounds with the protein or the peptide of claim 5; and

(b) selecting the one or more compounds that bind to [said] the protein or [said] peptide, wherein the compounds are ligands of the protein of claim 5.

8. (Amended) A method of screening for compounds that have an activity of inhibiting [the] binding between the protein of claim 5 and a ligand thereof, [said method] comprising [the steps of]:

(a) contacting the protein of claim 5 or a partial peptide thereof with the ligand in the presence of a test sample that includes one or more compounds and detecting a binding activity of [said] the protein or [said] partial peptide with [said] the ligand; and

(b) selecting the one or more compounds that reduce the binding activity detected in step (a) as compared with a binding activity detected in the absence of the test sample.

9. (Amended) A method of screening for compounds that [inhibit] suppress or enhance the activity of the protein of claim 5 to transduce a signal into a cell via the activation of the G protein of claim 5, [said method] comprising [the steps of]:



(a) contacting a ligand of [said] the protein of claim 5 with cells expressing [said] the protein in the presence of a test sample including one or more compounds,

(b) detecting an alteration in the cells that results from binding of [said] the ligand to [said] the protein, and

(c) selecting the one or more compounds that suppress or enhance the alteration detected in step (b) as compared with an alteration detected in the cells in the absence of the test sample.

10. (Amended) The method of claim[s] 8 or] 9, wherein the alteration in the cells is a change in cAMP concentration or calcium concentration.

12. (Amended) A compound isolated by the method of [any one of] claim[s] 7 [to 10].

16. (Amended) A method for diagnosing a disease selected from the group consisting of cancer, cirrhosis, and Alzheimer's disease, [said method] comprising [the steps of] detecting expression of the DNA of claim 1 in tissues related to the disease derived from a subject, or mutation in the DNA of claim 1 in the subject.

17. (Amended) [A] An agent for diagnosing [a disease selected from the group consisting of] cancer, cirrhosis, [and] or Alzheimer's disease, [said] wherein the agent [comprising] comprises the antibody of claim 11 [or the nucleotide of claim 15].

18. (New) A vector comprising the DNA of claim 2.

19. (New) A transformant comprising the DNA of claim 2.

20. (New) A transformant comprising the vector of claim 4.

21. (New) A protein or a peptide encoded by the DNA of claim 2.

22. (New) A compound isolated by the method of claim 8.

23. (New) A compound isolated by the method of claim 9.

24. (New) A compound isolated by the method of claim 10.

25. (New) An agent for diagnosing a cancer, cirrhosis, or Alzheimer's disease, wherein the agent comprises the nucleotide of claim 15.

26. (New) The method of claim 7, wherein the method is a method of screening for ligands that suppress or enhance an ability of the peptide of claim 5 to transduce a signal into a cell via activation of the peptide of claim 5.

27. (New) The method of claim 8, wherein the method is a method of screening for ligands that suppress or enhance an ability of the peptide of claim 5 to transduce a signal into a cell via activation of the peptide of claim 5.

# ABSTRACT

Nine novel genes sustaining hydrophobic domains, which are estimated to be seven transmembrane domains characteristic to G protein-coupled receptors, are successfully isolated by human tissue cDNA screening. These genes and proteins  
 5 which are the expression products thereof are usable in screening ligands, screening agonists or antagonists which are useful as drugs, diagnosing diseases in which these gene participate, etc.